

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Rene Gantier et al. Art Unit : 1631
Serial No. : 10/658,834 Examiner : Russell Scott Negin
Filed : September 8, 2003 Conf. No. : 7681
Title : RATIONAL EVOLUTION OF CYTOKINES FOR HIGHER STABILITY,
THE CYTOKINES AND ENCODING NUCLEIC ACID MOLECULES

Appendix



Cytokine regions susceptible to protease attack identified by structural alignment with Lead mutants of IFN α -2b

R

IFN- α 2b CDLPQTHSLGSRRTLMLLAQMRVLSLFSCLKDRHDFGPPQEEFGNQFQKAETIPVLHEMIQQIFNLFSSTKDSSAAWDETLDDKFYTELYQQLNDLEACVITQG
VGVTETPLMKEDSILAVRKYFQRITLYLKEKRYSPCAWEVVRRAEIMRSFSLSTNQLQESLRKSKE

Exemplary protein of the interferons/interleukin-10 family

IFN- β MSYNLLGFLQRSSNFQCKLLWQLNGRLEYCLKDRMNFDPPEEIKQLQFQKEDAAALTIYEMLQNIFAIFRQDSSSTGWNETIVENLLANVYHQINHLKTVLEEK
LEKEDFTRGKLMSSHLKRYYGRIHLHYLKAKEYSHCAWTIVRVEILRNFFYNRLTGTLRN

Exemplary protein of the short-chain cytokines family

EPO APPRLICDSRVLERYLLEAKEAENITTGCAEHC SLNENITVPDTRKYNFYAWKRMVEVGQAVEVWQGLALLSEAVLRGQALLVNSSQ PWEPLQLHVDKAVSGLRSL
TTLLRALGAQKEAISPPDDAASAAPLRTITADTFRKLFRVYSNFLRGKCLKLYTGEACRTGDR

Exemplary protein of the long-chain cytokines family

G-CSF TPLGPASSLPQSFLKCLQVRKIQDGAALQEKLVSECATYKLCHPPEELVLLGHSLGIPWAPLSSCPSSQALQAGCLSQLHSGLFLYQGLLQALEGISPELGPTLDTLQL
DVADFATTIWQQMEELGMAPALQPTQGAMPAFASAFQRRAGGVLVASHLQSFLEVSRYVLRHLAQP

FIG. 9

